



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY  
AND POLLUTION PREVENTION

June 3, 2015

MEMORANDUM

Subject: Acute Toxicity Review for EPA File Symbol 5813-RNI  
Data Package 425785  
Product Name: Clorox® WF

From: Wallace Powell, Biologist *WP*  
Chemistry and Toxicology Team  
Product Science Branch  
Antimicrobials Division (7510P)

Through: Karen Hicks, Team Leader  
Chemistry and Toxicology Team  
Product Science Branch  
Antimicrobials Division (7510P)

*QB for RPH 6/3/2015*

To: Demson Fuller, PM 32/ Wanda Henson  
Regulatory Management Branch II  
Antimicrobials Division (7510P)

Applicant: The Clorox Company

FORMULATION FROM PROPOSED LABEL:

<u>Active Ingredient:</u>	<u>% by weight</u>
Sodium hypochlorite (EPA PC Code 014703)	2.0
<u>Other Ingredient(s):</u>	<u>98.0</u>
Total:	100.0

BACKGROUND

In support of registration for the subject product, Clorox® WF, the applicant has submitted data support for acute oral, acute dermal, and acute inhalation toxicity, eye and dermal irritation, and dermal sensitization. The support consists of five submitted studies and, for eye irritation, a waiver request.

## RECOMMENDATION

The submitted studies, as listed in the table below, are acceptable. The identity of the test substance is confirmed in the applicant's 12/31/2014 letter. A review of each study is attached to this memorandum. The eye irritation data waiver request is acceptable based on the pH; the results of the dermal irritation study also support the waiver.

Summary. The acute toxicity profile of Clorox® WF is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	49525903	IV	Acceptable
Acute Dermal Toxicity	49525904	IV	Acceptable
Acute Inhalation Toxicity	49525905	IV	Acceptable
Primary Eye Irritation	49525906 (Waiver request)	I	Waived
Primary Dermal Irritation	49525907	I	Acceptable
Dermal Sensitization	49525908	Sensitizer	Acceptable

## Product Labeling

The Agency's *Label Review Manual* indicates for Clorox® WF the statement, "Remove and wash contaminated clothing before reuse," at the end of the human-hazard precautionary paragraph. However, the statement is shown in the submitted label as optional text.

The First Aid and human-hazard precautionary statements in the proposed labeling (version marked with date 12/9/2014) are otherwise acceptable.

The "Harmful if swallowed" precautionary statement and the "If Swallowed" First Aid statement are optional (and acceptable).

Note: This product meets the 40 CFR 157.22 criteria for child-resistant packaging.

Note: This product meets the 40 CFR 152.170(b) criteria for consideration of possible Restricted Use classification.

## DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OPPTS 870.1100)

**Product Manager:** 32  
**MRID No.:** 49525903

**Reviewer:** W. Powell  
**Study Completion Date:** 9/24/2014  
**Report No.:** 39141

**Testing Laboratory:** Product Safety Labs  
**Author:** Jennifer Durando

**Quality Assurance (40 CFR §160):** Included

**Test Material:** Clorox® WF, F2014.0078  
**Dosage:** 5,000 mg/kg

**Species:** Rat, Sprague-Dawley derived  
**Sex:** 3 Females  
**Age:** 8 weeks  
**Weight:** 134-146 grams  
**Source:** SAGE® Labs

**Method:** Up-and-Down Procedure. Limit test.

### Summary:

1. **Estimated LD<sub>50</sub>:** > 5,000 mg/kg
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

**Deviations from Guideline 870.1100 and other comments:** None noted.

### Results:

With administration of the test substance by gavage at a dose of 5,000 mg per kg body weight to female rats in a stepwise manner (first one rat and then, upon survival, two other rats), all three rats survived the 14-day observation period. The results indicate an acute oral LD<sub>50</sub> of greater than 5,000 mg/kg. Cage-side observations and gross necropsy revealed no notable findings. All three animals showed weekly weight gain.

#### Reported Mortality

Dosing Sequence	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	5,000	O	O
2	5,000	O	O
3	5,000	O	O

O = Survival

## DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OPPTS 870.1200)

**Product Manager:** 32  
**MRID No.:** 49525904

**Reviewer:** W. Powell  
**Study Completion Date:** 9/24/2014  
**Report No.:** 39142

**Testing Laboratory:** Product Safety Labs  
**Author:** Jennifer Durando

**Quality Assurance (40 CFR §160):** Included

**Test Material:** Clorox® WF, F2014.0078  
**Dosage:** 5,000 mg/kg

**Species:** Rat, Sprague-Dawley derived  
**Sex:** 5 Males and 5 Females  
**Age:** 8-9 weeks  
**Weight:** Males 255-275 grams, Females 152-180 grams  
**Source:** SAGE® Labs

### Summary:

1. **Estimated LD<sub>50</sub>:** > 5,000 mg/kg
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

**Deviations from Guideline 870.1200 and other comments:** None noted.

### Results:

Application of the test substance by dermal application at a dose of 5,000 mg per kg body weight to male and female rats produced no mortality during the 14-day observation period. The results indicate that the dermal LD<sub>50</sub> of the sample was greater than 5,000 mg/kg in male and female rats. Clinical signs noted were limited to dermal irritation signs in all animals between Days 1 and 12 (inclusive) and faint yellow stain at the dose site between Days 1 and 5 (inclusive). Necropsy revealed no gross abnormalities. All animals showed weekly weight gain.

### Reported Mortality

Dose Level (mg/kg)	Number Dead / Number Tested		
	Males	Females	Combined
5,000	0 / 5	0 / 5	0 / 10

## DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OPPTS 870.1300)

**Product Manager:** 32  
**MRID No.:** 49525905

**Reviewer:** W. Powell  
**Study Completion Date:** 9/24/2014  
**Report No.:** 39143

**Testing Laboratory:** Product Safety Labs  
**Author:** Jennifer Durando

**Quality Assurance (40 CFR §160):** Included

**Test Material:** Clorox® WF, F2014.0078  
**Concentration:** Gravimetric – 2.07 mg/L  
Nominal – 30.36 mg/L  
**Chamber Type:** Nose-only

**Species:** Rat, Sprague-Dawley derived  
**Sex:** 5 Males and 5 Females  
**Age:** 10 weeks  
**Weight:** Males 321-354 grams, Females 208-264 grams  
**Source:** SAGE® Labs

### Summary:

1. **Estimated LC<sub>50</sub>:** > 2.07 mg/L
2. **Average MMAD:** 2.12 µm
3. **Toxicity Category:** IV
4. **Classification:** Acceptable

**Deviations from Guideline 870.1300 and other comments:** None noted.

### Results:

All ten animals survived the 4-hour exposure and 14-day observation period. The median lethal concentration, then, is estimated to be greater than 2.07 mg/L in male and female rats. Clinical signs following exposure included hypoactivity, abnormal respiration, nasal discharge, ano-genital staining. All animals recovered by Day 6 and appeared active and healthy for the remainder of the study. All animals showed weekly weight gain during the observation period. Necropsy results were unremarkable.

### Reported Mortality

Exposure Concentration (mg/L)	Number of deaths / number tested		
	Males	Females	Combined
2.07	0 / 5	0 / 5	0 / 10

**Chamber Atmosphere**

Exposure Conc. (mg/L)	MMAD ( $\mu\text{m}$ )	GSD	% of Particles < 4.7 $\mu\text{m}$
2.07	2.12	2.01	88.5

**Chamber Environment**

Exposure Level (mg/L)	2.07
Chamber Volume (L)	28
Total Airflow Rate (Lpm)	36.0
Temperature ( $^{\circ}\text{C}$ )	22-23
Relative Humidity (%)	56-58

## DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OPPTS 870.2500)

**Product Manager:** 32  
**MRID No.:** 49525907

**Reviewer:** W. Powell  
**Study Completion Date:** 9/24/2014  
**Report No.:** 39144

**Testing Laboratory:** Product Safety Labs  
**Author:** Jennifer Durando

**Quality Assurance (40 CFR §160):** Included

**Test Material:** Clorox® WF, F2014.0078  
**Dosage:** 0.5 mL

**Species:** Rabbit, New Zealand albino  
**Sex:** 3 Females  
**Age:** Young adult  
**Weight:** 2.39 - 2.63 kg  
**Source:** Robinson Services, Inc.

### Summary:

1. **Toxicity Category:** I
2. **Classification:** Acceptable

**Deviations from Guideline 870.2500 and other comments:** None noted.

### Results:

Test material is evaluated as corrosive to the skin. Following a four-hour exposure in three rabbits, well-defined erythema was observed in all three animals (at the treated site) through 48 hours. Moderate edema was observed in two animals at 30-60 minutes and in one animal at 24 hours. At 72 hours, corrosion was observed in all three animals and the study was terminated for humane reasons.

#### Individual Dermal Irritation Scores following the four-hour exposure

Animal No.	Sex	Erythema / Edema			
		Time After Patch Removal			
		30-60 min	24 hrs	48 hrs	72 hrs <sup>1</sup>
3501	F	2 / 3 <sup>2</sup>	2 / 2 <sup>2</sup>	2 / 2 <sup>2</sup>	—
3502	F	2 / 3 <sup>2</sup>	2 / 3 <sup>2</sup>	2 / 2 <sup>2</sup>	—
3503	F	2 / 1	2 / 1 <sup>2</sup>	2 / 1 <sup>2</sup>	—

<sup>1</sup> Corrosion noted for all tested sites; study terminated.

<sup>2</sup> Area of discoloration.

## DATA REVIEW FOR DERMAL SENSITIZATION TESTING (OPPTS 870.2600)

**Product Manager:** 32  
**MRID No.:** 49525908

**Reviewer:** W. Powell  
**Study Completion Date:** 9/24/2014  
**Report No.:** 39145

**Testing Laboratory:** Product Safety Labs  
**Author:** Jennifer Durando

**Quality Assurance (40 CFR §160):** Included

**Test Material:** Clorox® WF, F2014.0078  
**Positive Control:** alpha-Hexylcinnamaldehyde, ≥ 95% (HCA)  
**Vehicle Control:** Propylene glycol

**Species:** Mouse, CBA/J, Female  
**Weight:** 16.3-21.2 g (Test and Control groups)  
**Age:** 9-10 weeks (Test and Control groups), 10-11 weeks (Preliminary Irritation Group)  
**Source:** The Jackson Laboratory (Test and Control groups),  
The Jackson Laboratory and Harlan Laboratories, Inc. (Preliminary Irritation Group)

**Method:** Local Lymph Node Assay

### Summary:

1. *Clorox® WF, F2014.0078* appeared to be a contact sensitizer.
2. **Classification:** Acceptable

**Deviations from Guideline 870.2600 and other comments:** None noted.

### Results:

Stimulation Index (SI) for each Test Substance group and for Positive Control group, was derived by dividing the average net DPM of each group by the average net DPM of the Vehicle Control group, where "net DPM" is measured DPM less background DPM.

Animal Group	Dose Preparation	Group Mean (Mean Net) DPM	Number of Mice	SI
Vehicle Control	Propylene glycol	1755.28	5	—
Positive Control	HCA, 25% w/w in propylene glycol	8476.25	5	4.83
Test Substance (1)	25% w/w in propylene glycol	2245.99	5	1.28
Test Substance (2)	50% w/w in propylene glycol	1835.49	5	1.05
Test Substance (3)	100% w/w in propylene glycol	28439.10	5	16.20

An SI well in excess of 3.0 was observed in the group treated with Test Substance 100% w/w in propylene glycol, thus indicating that *Clorox*<sup>®</sup> WF, F2014.0078 tested positive for dermal sensitization. Note: No erythema or edema were found at the test sites in any of the Test Substance groups or the Vehicle Control group, though desquamation was noted in three animals in the 100% Test Substance group on Day 6. The Positive Control group tested positive, as appropriate.